UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/412,268	10/05/1999	BEHNAZ PARHAMI-SEREN	MGH-1526	9455

21005 7590 12/20/2002

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/20/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/412,268	Applicant(s) Parhami-Seren et al
	Examiner Ungar	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 15, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above, claim(s) *7-37* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6 and 38-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The Amendment and Declaration filed October 15, 2002 (Paper No. 14) in response to the Office Action of April 9, 2002 (Paper No. 12) is acknowledged and has been entered. Previously pending claims 2, 3, 5, 6 and 38 have been amended and new claims 40-55 have been added. Claims 1-6, 38-55 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are maintained:

Claim Rejections - 35 USC § 101

4. Claims 2, 5, 6 remain rejected under 35 USC 101 and Claims 41-43 are rejected under 35 USC 101 for the reasons previously set forth in Paper No. 14, Section 3, pages 2-3.

As drawn to claims 2, 5, 6, Applicant argues that the Declaration shows that at 70 micromolar, digoxin inhibits the binding of the antibodies to ouabain and thus each antibody does not cross react with digoxin. However, the Declaration states that "when data points are so near to the X axis, that is near zero inhibition, it is possible that the data points are within the experimental error of the measurement method and therefore not truly different from zero." Dr. Hampert then declares that a two-tailed T test of the 70 micromolar point determined that when the inhibitor was digoxin at 50 and 100 mM, the result was p=0.16-0.18. This is not in fact different from zero inhibition. The argument has been considered but has not been found persuasive because Declaration is commensurate in scope with the data presented in the instant application. In the application, the data presented was

drawn to 70 micromolar, not millimolar, thus the Declaration is not commensurate in scope with the claimed invention. Further, since no datapoint was presented at 100 micromolar and "wobble" was found at 70 micromolar, it would be expected that inhibition would only increase from 70 to 100 micromolar. Given the information in the specification, it would not be expected that the binding of the antibodies to ouabain would not be inhibited by about 100 micromolar of digoxin and the invention appears to be inoperative.

As drawn to claims 41-43, the claims are drawn to antibody 5A12 wherein the antibody binds to ouabain and the binding of the antibody to ouabain is not inhibited by about 50 micromolar digoxin. A review of the specification, Figure 3 demonstrates that antibody 5A12 is inhibited by digoxin at less than about 50 micromolar digoxin. The invention appears to be inoperative. Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 112

5. Claims 2, 5, 6 remain rejected under 35 USC 112, first paragraph and Claims 41-43 are rejected under 35 USC 112 for the reasons previously set forth in Paper No. 14, Section 5, page 3.

Applicant reiterates arguments drawn to the rejection of the claims under 35 USC 101. The arguments have been considered but have not been found persuasive for the reasons set forth above. Further, as drawn to claims 41-43, since the embodiments are inoperative for the reasons set forth above, one of skill in the art would not know how to make and use the claimed invention with a reasonable

expectation of success. Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 2, 5, 6 remain rejected under 35 USC 112, first paragraph and Claims 41-43, 45-48, 53-55 are rejected for the reasons previously set forth in Paper No. 14, Section 6, pages 3-6.

Applicant argues that the formal requirements for biological deposit have been met. The argument has been considered but has not been found persuasive because a careful reading of the Deposit Declaration submitted reveals that Applicant has not addressed the issue draw to the replacement of the deposit if viable samples cannot be dispensed by the depository as required. Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 102

7. Claims 1, 3, 4, 39 remain rejected under 35 USC 102(b) and Claims 49-51 are rejected under 35 USC 102(b) for the reasons previously set forth in Paper No. 14, Section 10, pages 8-10.

Applicant argues as drawn to claims 1, 3, 4, 39 that the Lin reference antibody likely recognizes BSA and therefore would be expected to bind HSA and cites problems associated with double antigen immunization drawn to binding to the second antigen. The argument has been considered but has not been found persuasive because the claims are drawn to inhibition by digoxin and not to inhibition by BSA or HSA and it is clear that the plasma digoxin did not inhibit binding of the antibody to ouabain, thus the limitations drawn to digoxin inhibition are met absent evidence to the contrary that the claimed product is different from

that taught by the prior art and to establish patentable differences. Applicant is invited to submit objective evidence, demonstrating that the prior art antibody is different than the claimed antibody.

As drawn to claims 49-52, the claims are drawn to antibodies which have the same binding specificity as antibody 1-10, 7-1, 8E4, all of which bind ouabain. As previously disclosed, the antibody of Lin et al binds ouabain. All of the limitations of the claims are met.

Claim Rejections - 35 USC § 103

8. Claims 1, 3, 4, 38, 39, 44 remain rejected under 35 USC 103 for the reasons previously set forth in Paper No. 14, Section 12, pages 11-13.

Applicant argues (a) Blaustein et al do not teach any antibody having binding specificity for ouabain but teach cross reactivity to well known steroids, (b) reiterates arguments drawn to Lin et al, (c) state that Blaustein et al do not teach a monoclonal antibodies but only exemplify a polyclonal antibody, (d) the combined teachings of Blaustein et al and Lin et al would destroy the intent, purpose or function of the Blaustein et al reference and therefore the obviousness rejection is not proper and cites *In re Gordon*, (e) even if the improper combination was made, Applicant tried the method of Blaustein in an attempt to obtain a monoclonal antibody having binding specificity for ouabain and encountered problems, (f) the teachings of Blaustein, 1996, do not remedy the defects of the combined references.

The arguments have been considered but have not been found persuasive because (a')(c') the references in combination make the claimed invention obvious for the reasons of record, (b') the arguments are not persuasive for the reasons set

forth above, (d') the cited court decision is not relevant to the instant invention because a review of *In re Gordon* revealed that the application was drawn to a blood filter assembly for use during medical procedures wherein both the inlet and outlet for the blood were located at the bottom end of the filter assembly, and wherein a gas vent was present at the top of the filter assembly which is not an art analogous to the antibody art claimed in the instant invention, (e') Examiner takes note that binding specificity of an antibody resides in epitope selectivity, it is clear that the antibody of the combined references binds to an epitope on ouabain and therefore has binding specificity for ouabain, (f') the references in combination make obvious the claimed invention for the reasons of record.

New Grounds of Objection

9. Applicant is advised that should claims 38 be found allowable, claim 44 will be rejected under 35 U.S.C. 101 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

New Grounds of Rejection

Claim Rejections - 35 USC § 112

10. Claims 1, 3, 4, 38, 39, 44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The

written description in this case only sets forth antibody species, 1-10, 5A12, 7-1, 8E4 and therefore the written description is not commensurate in scope with the claims drawn to antibodies that bind to ouabain but do not crossreact with digoxin.

Although the specification claims antibodies that bind ouabain which are not inhibited by 100 micromolar digoxin, and specifically states that the specific antibodies claimed and exemplified do not cross react with digoxin, the data presented in the specification clearly shows that the antibodies exemplified do cross react with digoxin and for the reasons set forth above would be expected to cross react with 100 micromolar digoxin. The instant disclosure of these cross reacting species of antibodies does not adequately describe the scope of the claimed genus, which encompasses all antibodies that do not cross react with digoxin. Although drawn to the DNA art, the findings of the court in *Regents of the University of California v. Eli Lilly &* is clearly relevant to the instant rejection. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). For the reasons set forth above, it appears that the instant disclosure does not describe a single monoclonal antibody that binds to ouabain which is not inhibited by 100 micromolar digoxin. One of skill in the art would reasonably conclude that the inventor(s), at the time the application was filed, did not have possession of the claimed invention.

11. Claims 1-4, 6, 38, 40-44 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "about 100 micromolar" and "about 50 micromolar"has no clear support in the specification and the claims as originally filed. Applicant points to page 22, line 20 of the specification to support the limitation of "about 100 micromolar. However, a review of the cited support reveals support for the antibody 5A12, 7-1, 1-10 not being inhibited with concentrations "as high as 100 micromolar", further, there is no mention of Antibody 8E4 not being inhibited by concentrations "as high as 100 micromolar. The suggested support is not found persuasive. Further, applicant points to originally filed claims 1, 2, 5, 6, 38 and figure 3 for support for the newly claimed limitation of "about 50 micromolar". However, a review of the cited support reveals no limitation in the cited claims for "about 50 micromolar" and nothing in figure 3 that points specifically to the newly claimed limitation. The suggested support is not found persuasive. The subject matter claimed in claims 1-4, 38, 40-41, 43-44 broadens the scope of the invention as originally disclosed in the specification.

12. All other objections and rejections recited in Paper No. 14 are withdrawn.

13. No claims allowed.

14. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1640.

Susan Ungar
Primary Patent Examiner
December 12, 2002